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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/572,543

11/28/2006

Darcey Clark

X-17671

7392

25885 7590 08/27/2008

ELI LILLY & COMPANY

PATENT DIVISION

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EXAMINER

STONE, CHRISTOPHER R

ART UNIT

PAPER NUMBER

1614

NOTIFICATION DATE

DELIVERY MODE

08/27/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No. 10/572,543	Applicant(s) CLARK ET AL.	
	Examiner CHRISTOPHER R. STONE	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 74-81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 74-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed May 27, 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 74-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keegan et al (WO 02/07094, provided by Applicant) in view of Gandhi et al (provided by Applicant).

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Claims 74-81 are drawn to a method of treating a cell proliferative disorder comprising administering a Chk1 activator, followed by a selective Chk1 inhibitor. Gemcitabine, compound 281 (p. 145, WO 2002070494) and non small cell lung cancer are the elected species of Chk1 activator, Chk1 selective inhibitor and cell proliferative disorder currently under examination.

Keegan et al teaches the administration of gemcitabine and compound 281 for the treatment of human non small cell lung cancer (p. 35, line 21; p. 49, line 33; p. 145, compound 281). Compound 281 is further taught to enhance the therapeutic benefit of chemotherapy with compounds such as gemcitabine (p. 45, lines 19-24; p. 49, line 33; p. 145, compound 281). Keegan et al does not teach the administration of gemcitabine for from about 30 minutes to about 96 hours or the administration of gemcitabine for from about 30 minutes to 48 hours. Gandhi et al teaches the administration of gemcitabine for twelve hours without untoward toxicity (abstract). Gandhi further teaches that this prolonged infusion derives the maximum cytotoxic advantage (p. 671, right column, paragraph 2). Therefore it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to administer gemcitabine for 12 hours, in order to obtain the maximum cytotoxic effect. Keegan et al does not teach the administration of compound 281 for from up to about 1 hour to up to about 72 hours following the administration of gemcitabine; however Keegan does teach that gemcitabine and compound 281 can be administered in multiple doses at different intervals (p. 50, lines 20 and 21). Therefore, it would have been obvious for one of ordinary skill in the art at the time of the instantly claimed invention to optimize

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the sequence of administration and infusion duration to determine the regimen with maximum efficacy, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. Such routine experimentation is common in the pharmaceutical art. Additionally, Keegan does not explicitly teach that the administration of gemcitabine synchronizes cell cycle arrest among the tumor cells; however this is a property of the composition and is necessarily present. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Applicant argues that Keegan et al does not teach the administration of gemcitabine prior to the administration of compound 281. This is found unpersuasive because Keegan et al explicitly teaches that the Chk1-inhibitor compound (e.g. compound 281) can be administered before, during or after administration of the chemotherapeutic agent, e.g. gemcitabine (p. 45, lines 14-18). Additionally Keegan et al teaches that the determination of the exact formulation, route of administration, dosage and schedule is chosen by the individual physician, based on factors such as patient age, weight, response, etc. and is within the ordinary skill in the art, i.e. does not require undue burden (p. 42, lines 16-22 and p. 50, lines 7-30). Additionally, Applicant is reminded of *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1217-18 [18USPQ2d 1016]

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(Fed.Cir. 1991) which affirmed that the use of the word “about” in a claim is appropriate where the claim contains a range of components with no absolute boundaries and that the use of the word “about” in a claim is only limited to the extent that prior art exists, that is, prior art which would limit broad interpretation of the claim. *Id.* at 1218. In the instant case, the claims teach that there is no exact duration of administration of the active agents necessary to practice the instantly claimed invention. Additionally, there is no prior art teaching that limits the duration of administration. Therefore, the instant claims only require that compound 281 be administered any time after gemcitabine and, as noted above, this method is disclosed in Keegan et al.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

22August2008
CRS

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614